UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/086,294	02/28/2002	Loretta Nielsen	016930-003712US	3210

20350 7590 03/26/2007

TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER	
HAMA, JOANNE	
ART UNIT	**PAPER NUMBER**
1632	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/086,294	NIELSEN ET AL.	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-5,10-22,25-28,30-40 and 78-80* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *37-40* is/are allowed.

6)☒ Claim(s) *1,3-5,10-22,25-28,30-34 and 78-80* is/are rejected.

7)☒ Claim(s) *35 and 36* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant filed a response to the Non-Final Action of July 5, 2006 on January 5, 2007. Claims 2, 6-9, 23, 24, 29, 41-77 are cancelled. Claims 1, 20-22, 25, 27, 28, 30, 35, 37, 78, 80 are amended.

Claims 1, 3-5, 10-22, 25-28, 30-40, 78-80 are under consideration.

Withdrawn Rejections

35 U.S.C. § 112, 2nd parag.

Applicant's arguments, see page 9 of Applicant's response, filed January 5, 2007, with respect to the rejection of claims 20-22, 25-30, 35, 37 have been fully considered and are persuasive. Applicant indicates that claims 20-22, 25, 27, 28, 30, 35, 37 do not recite administration of protein. Applicant indicates that claim 29 is cancelled. The rejection of claims 20-22, 25, 27-30, 35, 37 has been withdrawn. Applicant indicates that claim 26 appear to have been inadvertently included in the rejection as the claim does not recite administration of protein. In response, claim 26 was inadvertently included in the rejection. The rejection of claim 26 is withdrawn.

35 U.S.C. § 102(b)

Applicant's arguments, see Applicant's response, filed January 5, 2007, with respect to the rejection of claims 1, 3, 10, 18-22, 25-28, 31, 78-80 have been fully considered and are persuasive. Applicant indicates that Tocque, U.S. Patent 6,262,032

is not 102(b) art. The rejection claims 1, 3, 10, 18-22, 25-28, 31, 78-80 has been withdrawn.

35 U.S.C. § 103(a)

Applicant's arguments, see page 12-13, filed January 5, 2007, with respect to the rejection of claims 1, 3, 4, 10, 18-22, 25-28, 31, 35, 36, 78-80 have been fully considered and is persuasive. Applicant has amended the claims and Gjerset's teaching does not render the claimed invention obvious. It is noted, for example, that Gjerset does not specifically teach that the adenoviral vector comprising the nucleic acid sequence is injected into the tumor. The rejection of claims 1, 3, 4, 10, 18-22, 25-28, 31, 35, 36, 78-80 has been withdrawn.

New/Maintained Rejections/Objections

Claim Objections

Claim 79 is newly objected to because of the following informalities: claim 79 includes non-elected subject matter, treatment using p53 protein. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 80 remains rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

1) an *in vivo* method for reducing the size of a tumor in a mammal comprising mammalian cancer cells deficient in functional p53, said method comprising directly contacting cancer cells with an adenoviral vector comprising a nucleic acid encoding p53, and also contacting said cells with a microtubule affecting agent, wherein the microtubule affecting agent comprises a taxane, such that growth of said cancer cells is reduced and/or said cancer cells undergo apoptosis,

does not reasonably provide enablement for

1) an *in vivo* method of treating mammalian cancer cells deficient in functional p53, wherein said method comprises contacting cancer cells with an adenoviral vector comprising a nucleic acid encoding p53, wherein said vector is administered directly, and contacting said cells with a taxane, such that one or more disease characteristic of the cells is ameliorated, wherein the mammalian cancer cells are human head and neck, ovarian, prostate, or mammary cancer cells.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for reasons of record, December 5, 2005 and July 5, 2006.

Applicant's arguments filed January 5, 2007 have been fully considered and they are persuasive in part.

Applicant indicates that claim 80 has been amended. However, this is not persuasive because as indicated in the Office Action, July 5, 2006, page 6, the specification does not provide guidance for the treatment of metastatic cancer. Note that claim 80 is readable on metastatic cancer. As such, the rejection as it applies to this claim remains.

With regard to claims 1, 37, 78, Applicant has amended the claims such that the invention is drawn to an in vivo method of reducing the size of a tumor, wherein the tumor is directly injected with an adenoviral vector (or a DNA vector) comprising a nucleic acid sequence encoding functional p53. The rejections as they applied to these claims are withdrawn. It is noted that the rejection of claims 3-5, 10-22, 25-28, 30-36, 38-40, which depend on claims 1 or 37 are withdrawn, as the amendments to the independent claims now enable the dependent claims.

With regard to claim 79, Applicant indicates that claim 79 is drawn to an in vitro method and the Office Action of December 5, 2005 indicated that in vitro embodiments were enabled. Applicant indicates that the rejection of claim 79 appears to be a clerical error. In response, the inclusion of claim 79 was a clerical error. The rejection of claim 79 is withdrawn.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30, 33 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 30 is unclear. Claim 30 indicates that the administration of the vector is intraperitoneally. However, it is unclear how intraperitoneally is the same scope as "direct injection" of claim 1. It is noted that while the ovaries are in the region in which intraperitoneal injections occur, this does not mean that the intraperitoneal injections that occur in claim 30 are necessarily limited to direct injection to the ovary.

Claim 33 is unclear. Claim 33 indicates that contacting comprises a wide variety of administration routes. However, it is unclear how routes such as "systemic" injection of claim 33 is the same scope as "direct" administration in claim 1.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3, 10, 18-22, 25-28, 31, 32, 78-80 are newly rejected under 35 U.S.C. 102(e) as being anticipated by Tocque, U.S. Patent 6,262,032, patented July 17,

2001, see IDS as evidenced by Brown et al., 1991, Journal of Clinical Oncology, 9: 1261-1267.

Note that there is no rejection of the claims under 35 U.S.C § 103, using this reference.

Tocque teaches a method of destroying a hyperproliferative cell in a tumor of an animal comprising administering a transgene construct comprising a nucleic acid sequence encoding p53 and a chemotherapeutic agent. Tocque teach H460 cells were transfected *in vitro* with a cDNA coding for the wild-type p53 protein placed in a plasmid under the control of a CMV promoter and were further treated with taxotere (Tocque, Example 3). Tocque teaches that the treatment with the p53 vector and taxotere reduce the number of H460 colonies more than by a treatment with taxotere only (Tocque, Fig. 3B). Further, Tocque also teaches that Example 3 demonstrates that cells treated with p53 vector and taxotere die at concentrations which are ineffective on cells that do not express wild-type p53 (Tocque, col., 7, 5th parag.). While Tocque teach one type of cells, Tocque contemplates that that the method is applied to cancer cells from a variety of tissues, including colon, thyroid, and myeloid leukaemias (Tocque, col. 4, 6th parag.). Tocque teaches that the vector comprising a nucleic acid sequence encoding p53 and a taxane can be administered *in vivo* by intratumoral injection and that in order to obtain a maximum expression in a maximum number of dividing cells, administration of the transgene is repeated (Tocque, col. 13, parag. under "Administration Protocol", see also claims). In addition to plasmid, Tocque teaches the use of adenoviral vector (Tocque, col. 10, lines, 41-42, also see claims).

Tocque teaches that the nucleic acid vector is in an injectable form and thus is in a vehicle which is pharmaceutically acceptable for injection (Tocque, col. 4, 1st parag.). Tocque teaches that the two agents (nucleic acid vector and chemotherapeutic agent) may be used simultaneously, separately, or spread over time (Tocque, col. 4, 3rd parag.).

Regarding the administration of the chemotherapeutic agent (e.g. taxol), Tocque teaches that the chemotherapeutic agent is administered according to the clinical protocols in force (Tocque, col., 13, under Administration Protocol). According to Brown et al., taxol can be administered intravenously (Brown et al., see title and abstract). As such, Tocque has support for intravenous administration of taxol.

Thus, Tocque anticipate claims 1, 3, 10, 18-22, 25-28, 31, 32, 78, 79, 80.

Applicant's arguments filed January 5, 2007 have been fully considered but they are not persuasive.

With regard to Tocque teaching that in the alternative, the claims are obvious, Applicant indicates that amended independent claims 1, 78-80 encompass methods for treating human head and neck, ovarian, prostate, and breast cancer cells and that Tocque describes a treatment of H460 lung cells and contemplates the potential treatment of certain other adenocarinomas (col. 4, lines 52-63) (Applicant's response, page 9, 2nd parag. under "Tocque does not render the claims obvious"). In response, the rejection has been modified and the claims are rejected under 102 as being anticipated. As such, "reasonable expectation of success" is not applicable to the

rejection. The claims in the patent indicate that Tocque is enabled for the breadth of hyperproliferative cells. While Tocque teach one kind of cancer cell, Tocque indicates as to what kind of cancer cell can be treated with the claimed method (i.e. the cancer cells are p53 negative and hyperproliferative).

Applicant indicates that there is no indication in Tocque that the artisan would have reasonable expectation of success for the presently claimed treatments. Applicant indicates that cancer is a complex disease and that combination therapy for cancer treatment can be complex in nature and not all combinations can be predicted to work equally effectively (Applicant's response, page 10, under "No expectation of success"). In response, the rejection, above is a 102 and thus, "reasonable expectation of success" is not applicable to the rejection. Tocque teaches a method of destroying a hyperproliferative cell, wherein the cell is deficient in functional p53, and wherein the method comprises direct administration of an adenoviral vector comprising the nucleic acid sequence encoding p53 and a taxoid (Tocque, col. 7, 5th parag., see also claims). Tocque teaches the same method as that claimed and provides the parameters to make the method work in the specification; note also that the claims in Tocque are drawn to any hyperproliferative cell. In addition to this issue, while Applicant has provided an assertion, Applicant has not provided evidence that the method taught by Tocque is not enabled for the specifically claimed method using cells of human head and neck, ovarian, prostate, or mammary cancer cells that lack functional p53. If Applicant questions the enablement of the patent, Applicant's attention is directed to 35 U.S.C. 282, wherein a patent is presumed valid. As such, Tocque's claims are enabled.

Applicant indicates that the instantly claimed treatment is not obvious because the combination exhibits surprising and unexpected results. In particular, the publication by Nielsen et al., 1998 teaches that there is a synergistic effect following administration of p53 and paclitaxel (Applicant's response, page 10, under Surprising Results). In response, the rejection is a 102 and not a 103. Thus, unexpected results cannot overcome a 102. Tocque teaches the same steps as those instantly claimed. While Tocque does not specifically teach that there was any synergistic effect between the combination of the adenovirus comprising p53 and a taxoid, that effect would have been inherent to the method taught by Tocque. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 10-13, 15-17, 34 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Tocque in view of Gregory et al. U.S. Patent 5,932,210, patented August 3, 1999, for reasons of record, July 5, 2006.

Applicant's arguments filed January 5, 2007 have been fully considered but they are not persuasive.

Applicant indicates that there is no teaching or suggesting in Tocque that the artisan would have a reasonable expectation of success of treating head and neck, ovarian, prostate, and breast cancer cells with a nucleic acid sequence encoding p53 in combination with a taxane (Applicant's response, page 11, under Second Rejection Under Section 103). In response, this is not persuasive because as indicated above, Tocque teaches the same steps as that described in the claims and also indicates what characteristic a cancer cell has (i.e. p53 mutant) such that the invention is used to treat these cancer cells. Thus, the rejection is maintained.

Applicant indicates that claim 2 was rejected and appears to have been included inadvertently. In response, claim 2 was included inadvertently.

It is noted that the rejections of 18-22, 25-28, 31, 78-80 are withdrawn because they have already been rejected above in the 102 rejection. Gregory does not provide any further guidance to render these claims obvious.

Claims 1, 10, 11, 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tocque in view of Gregory et al. U.S. Patent 5,932,210, patented August 3, 1999, for reasons of record, July 5, 2006.

Applicant's arguments filed January 5, 2007 have been fully considered but they are not persuasive.

Applicant indicates that there is no teaching or suggesting in Tocque that the artisan would have a reasonable expectation of success of treating head and neck, ovarian, prostate, and breast cancer cells with a nucleic acid sequence encoding p53 in combination with a taxane (Applicant's response, page 11, under Second Rejection Under Section 103). In response, this is not persuasive because as indicated above, Tocque teaches the same steps as that described in the claims and also indicates what characteristic a cancer cell has (i.e. p53 mutant) such that the invention is used to treat these cancer cells. Thus, the rejection is maintained.

Applicant indicates that claim 2 was rejected and appears to have been included inadvertently. In response, claim 2 was included inadvertently.

It is noted that the rejections of 12,13, 15-22, 25-28, 31, 34, 78-80 are withdrawn because they have already been rejected above in the 102 rejection. Gregory does not provide any further guidance to render these claims obvious.

Claims 1, 4, 5 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Tocque, U.S. Patent 6,262,032, patented July 17, 2001, see IDS, and in view of Roth and Cristiano, 1997, Journal of the National Cancer Institute, 89: 21-39, previously

cited, as evidenced by Shea, 1997, Cancer Chemother. Pharmacol., 40 (Suppl.): S74-S78.

As discussed above, Tocque teaches an in vivo method of destroying a hyperproliferative cell in a tumor of an animal comprising administering a transgene construct comprising a nucleic acid sequence encoding p53 and a chemotherapeutic agent. While Tocque provide this teaching, Tocque does not teach a step of including a third chemotherapeutic agent.

Roth and Cristiano teach that gene therapies for cancer can be used in combination with surgery, radiation therapy, and chemotherapy as gene therapies interact in synergistic or additive ways with them. As a whole, studies that teach combination therapy indicate that improved methods for treating cancer can be achieved by combining conventional cancer treatments and gene therapy for greater therapeutic effect (Roth and Cristiano, page 28, 1st col., parag. under Interactions with Other Cancer Therapies). As for the use of cisplatin, carboplatin, or navelbine, these chemotherapeutic compounds were well known at the time of filing (e.g. see Shea reference) and an artisan would have readily used any of them as an additional chemotherapeutic agent (see claim 5).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to include an additional step of adding a chemotherapeutic agent such as cisplatin, carboplatin, or navelbine to the method taught by Tocque.

One having ordinary skill in the art would have been motivated to include an additional step of adding a chemotherapeutic agent because the art teaches that combination therapy (e.g. such as that taught by Roth and Cristiano) is commonly used in cancer treatment.

There would have been a reasonable expectation of success given the Tocque for teaching a method of destroying hyperproliferative cells using adenoviral p53 and a taxane and Roth and Cristiano for teaching that combination therapy is a common way of treating cancers.

The instant situation is amenable to the type of analysis set forth in In re Kerkhoven, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to produce a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Given the teaching of the prior art compositions of expression vectors encoding p53 protein, a microtubule affecting agent (i.e. a taxane), and other chemotherapeutic agents-all taught to be useful for the treatment of cancer, it would have been prima facie obvious to one of ordinary skill in the art to combine these compositions to generate a new composition for the treatment of cancer with a reasonable expectation of success.

Conclusion

Claims 37-40 are allowable.

Claims 35, 36 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 1, 3-5, 10-22, 25-28, 30-34, 78-80 remain rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has

been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

JH

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER